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Original Article

Rapid eye movement sleep behaviour disorder in young- and older-onset Parkinson disease: a questionnaire-based study

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ABSTRACT

Background: Rapid eye movement sleep behavior disorder (RBD) is common in Parkinson disease (PD).
Objectives: To determine the frequency of clinically probable RBD (cpRBD) in young-onset (21 to ⩽40 years; YOPD) and older-onset PD (>40 years; OOPD) and characterize its pattern.
Methods: A total of 156 patients with PD (YOPD-51, OOPD-105) were clinically examined and the presence of RBD was diagnosed using the minimal criteria for diagnosis of RBD (International Classification of Sleep Disorders, ICSD-1). RBD screening questionnaire based on the minimal criteria was used. The bed-partners were also interviewed with Mayo sleep questionnaire. Other scales included Unified Parkinson Disease Rating Scale part III (UPDRS III), Hoehn & Yahr stage, Mini Mental Status Examination, Pittsburgh Sleep Quality Index, Parkinson Disease Sleep Scale, Epworth Sleep Scale, Hamilton Anxiety Rating Scale and Hamilton Depression Rating Scale.
Results: cpRBD was diagnosed in 30 (19.2%) patients, majority being OOPD rather than YOPD (86.7% vs 13.3%; $P = 0.01$). The frequency of RBD was significantly higher ($P = 0.016$) in OOPD (24.8%) compared to those with YOPD (7.8%). Most often (72.4%) RBD occurred after the onset of parkinsonian symptoms. RBD was independently associated with higher global PSQI scores, total ESS scores and total PDSS scores after adjusting for the effects of age, gender, Hoehn & Yahr stage and duration of illness.
Conclusions: Patients with RBD were older with later-onset motor symptoms, a more advanced stage, poorer sleep quality, and more frequent daytime sleepiness. Older-onset PD had a higher frequency of RBD than young-onset PD.

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1. Introduction

Parkinson disease (PD) is one of the most widespread neurodegenerative disorders. Apart from the disabling motor symptoms which are amenable to treatment, patients also suffer from several non-motor symptoms such as depression, anxiety, psychosis, and dementia [1]. Sleep disturbances occur in up to 98% of patients with PD, ranging from insomnia to parasomnias [2].

Rapid eye movement (REM) sleep behavior disorder (RBD) is one of the sleep parasomnias characterized by violent dreams and the subsequent acting out of dreams during REM sleep [3]. RBD is often associated with α-synucleinopathies, particularly PD. The prevalence of RBD in the general population is 0.5% [4] and in PD is variable from 15% to 72% [5–8].

Several studies are available from western countries on the prevalence of RBD, its clinical characteristics, and its association with other non-motor symptoms of PD such as psychosis (hallucinations and delusions) and dementia. However, the literature on the frequency of RBD in PD in the Indian subcontinent is scant [9]. It is possible that there may be a difference in the cultural perception of dreams and genetic factors that can influence sleep architecture. Studies on the frequency of RBD in young-onset PD are limited [10,11]. Hence the present study was undertaken primarily to determine the frequency of clinically probable RBD (cpRBD) in PD, and to compare the frequency of cpRBD between two groups of PD patients: young-onset PD (age at onset of motor symptoms 21–40 years; YOPD) and older-onset PD (age at onset of motor symptoms >40 years; OOPD) [12]. The secondary objective was to compare the clinical characteristics of patients with cpRBD between the two groups of PD patients, albeit that this study was questionnaire-based with lack of polysomnographic confirmation of RBD.

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2. Methods

2.1. Patients and setting

The study included 156 consecutive patients with PD (mean age, 55.4 ± 11.2 years) who visited the neurology outpatient services, and movement disorder clinic as well as those admitted in the neurology ward of the National Institute of Mental Health and Neurosciences (NIMHANS) in Bangalore, India. PD was diagnosed according to the UK Parkinson Disease Society Brain Bank criteria (Queen Square Brain Bank criteria) [13,14]. The patients admitted in the ward were for adjustment of medications and no one had delirium. The study period was from October 2010 to December 2011 and was approved by the Institute Ethics Committee. All subjects gave written informed consent after full explanation and detailed description of study method. The patients presenting with features of parkinsonism were clinically examined to rule out Parkinson-plus syndromes and only those patients (n = 156) fulfilling the inclusion criteria for PD and consenting to participate in the study were recruited. Based on the age of onset of motor symptoms of PD, they were grouped into young- and older-onset PD. All 156 patients were interviewed by one of the authors (R.M.). No incentives were offered for participation. The study was prospective, cross-sectional, and hospital-based.

2.2. Investigations

All patients were interviewed and examined with documentation of demographic variables, disease profile including age at onset of motor and non-motor symptoms, and treatment profile. The staging of PD was done using modified Hoehn & Yahr Stage (H&Y) [15], the severity of motor symptoms of PD was assessed using Unified Parkinson Disease Rating Scale part III (UPDRS-III) [16], and cognitive function was assessed using the Mini Mental Status Examination (MMSE) scale [17]. The total levodopa equivalent dose (TLED) was calculated for each patient [18].

Evaluation of sleep was carried out using the Parkinson Disease Sleep Scale (PDSS) [19], Pittsburgh Sleep Quality Index (PSQI) [20] and Epworth Sleepiness Scale (ESS) [21]. In addition, all patients were interviewed with RBD screening questionnaire (RBDSQ) [22] – a well-validated diagnostic screening tool for RBD. The RBDSQ is a 10-item questionnaire, and cut-off value of five points was used to diagnose clinically probable RBD (cpRBD). The bed partner or spouse of all the patients was interviewed with Mayo Sleep Questionnaire (MSQ) question 1, which pertains to RBD. This was used to confirm cpRBD in patients who were unable to recall the sleep-related events. RBDSQ is based on the minimal criteria (criteria B + C) of International Classification of Sleep Disorders (ICSD-1) [23] for the diagnosis of RBD [(B) Limb or body movement is associated with dream mentation. (C) At least one of the following occurs: (criterion C1) harmful or potentially harmful sleep behaviors; (criterion C2) dreams appear to be 'acted out'; (criterion C3) sleep behaviors disrupt sleep continuity]. The details about timing of dream enactment and clinical events were obtained based on structured clinical interview.

Hamilton Anxiety Rating Scale (HAM-A) [24] and Hamilton Depression Rating Scale (HAM-D) [25] were used to assess anxiety and depression respectively.

The following subscores of UPDRS III were calculated for all patients: (i) tremor score (UPDRS 20, 21, maximum score 28); (ii) rigidity score (UPDRS 22, maximum score 20); (iii) bradykinesia score (UPDRS 23–26, 31 maximum score 36); (iv) gait/postural stability score (UPDRS 27–30, maximum score 16); (v) bulbar abnormalities score (UPDRS 18, 19, maximum score 8); (vi) axial signs score (UPDRS 18–19, 22, 27–30, maximum score 42); and (vii) limb signs score (UPDRS 20–26, maximum score 84). The proportion of UPDRS III motor scores accounted for by each subscore was determined. For tremor score (% of UPDRS III), the tremor score was divided by the total UPDRS III score. Similar derivations were made to assess the proportion accounted by rigidity, bradykinesia, gait/postural stability, and bulbar abnormalities [3]. The tremor-dominant subtype of PD was defined as patients with a ratio of tremor to bradykinesia score (bradykinesia, rigidity and postural instability subscore from the UPDRS motor scale) of $\geqslant$0.5, and the akinetic rigid subtype as patients with a ratio of <0.5 [26].

2.3. Statistical analysis

The data were analyzed using SPSS version 16.0. The qualitative data were analyzed using χ^2-test or Fisher's exact test. The continuous variables were expressed as mean ± standard deviation and categorical variables as frequency and percentage. The normality of the distribution was assessed by the skewness of the values. For the analysis of continuous variables, non-parametric testing (Mann–Whitney test and Wilcoxon's test) was employed. $P < 0.05$ was taken as statistically significant. Correlation among various clinical parameters and scales employed in the study to determine the significance was done using Spearman's correlation coefficient.

3. Results

In all, 156 PD patients (51 YOPD and 105 OOPD) were recruited during the study period. There were 30 patients with cpRBD (19.2%). The frequency of cpRBD was significantly higher (P = 0.016) in OOPD (24.8%) compared to those with YOPD (7.8%). In majority of the patients (72.4%) the symptoms of RBD appeared after the onset of motor symptoms of parkinsonism. In the remainder, it appeared either before (20.7%) or along with parkinsonism (6.9%). Due to low frequency of cpRBD in YOPD patients, a comparison with cpRBD in OOPD was not carried out.

3.1. Demographic features and clinical characteristics

Patients with cpRBD were significantly older and had later age at onset of motor symptoms of PD (Table 1). There was no difference between the two groups (cpRBD and non-cpRBD) with respect to gender distribution (70.0% vs 77.8% men). Two patients with cpRBD had familial PD whereas 18 patients without cpRBD had familial PD. The duration of symptoms, duration of treatment, and TLED (mg/day) were higher in the cpRBD group compared to those without cpRBD, but these differences were not statistically significant. There was no significant difference between the groups with respect to the motor subtypes of PD.

3.2. Rating scores and disease complications

The mean UPDRS III motor score was similar in both groups (Supplementary Table 1). The mean tremor score was lower in the cpRBD group but was not statistically significant. The gait/postural stability score (% of UPDRS III) was significantly higher (15.4 ± 6.2% vs 13.3 ± 6.5%; P = 0.04). Patients with cpRBD had higher mean axial:limb sign ratio, which was statistically significant. There was no significant difference with respect to the mean rigidity or mean bradykinesia score. The median H&Y stage in the cpRBD group was 2.5, which was higher than in the non-cpRBD group (P = 0.02). The percentage of patients with cpRBD with advanced stage of PD was high (H&Y stage $\geqslant$2.5). The percentage of patients with falls and dyskinesia were similar in both groups. The mean HAM-A and HAM-D scores were similar in both groups.

Table 1
Clinical characteristics of patients with and without cpRBD.

Characteristics	cpRBD (n = 30)	Non-cpRBD (n = 126)	P-value
Age (years)	61.1 ± 9.8	54.1 ± 11.1	0.04
Men (%)	21 (70.0)	98 (77.8)	0.35
Duration of disease (years)	6.3 ± 4.8	5.6 ± 4.6	0.40
Age at onset of PD (years)	54.8 ± 10.7	48.6 ± 12.3	0.01
Parkinson disease			
YOPD (%)	4 (13.3)	47 (37.3)	0.01
OOPD (%)	26 (86.7)	79 (62.7)	
Duration of treatment (months)	53.8 ± 51.0	43.5 ± 42.9	0.78
TLED (mg/day)	662.9 ± 427.2	582.5 ± 327.7	0.51
Familial PD (%)	2 (6.7%)	18 (14.3%)	0.36
Tremor type PD (%)	13 (43.3%)	60 (47.6%)	0.69
Akinetic rigid type PD (%)	17 (56.7%)	66 (52.4%)	–

cpRBD, clinically probable rapid eye movement sleep behavior disorder; PD, Parkinson disease; YOPD, young-onset PD; OOPD, older-onset PD; TLED, total levodopa equivalent dose.
Values expressed as mean ± SD or number (%).

3.3. Sleep scales

PD patients with cpRBD had significantly higher sleep disturbances (Table 2). The global PSQI was significantly worse in patients with cpRBD. Patients with cpRBD were poor sleepers (83.3% vs 38.1%; $P = 0.0001$). The total ESS score was significantly higher in patients with cpRBD with a significantly higher percentage of patients with excessive daytime sleepiness (60.0% vs 20.4%; $P < 0.0001$). The total PDSS was also significantly worse in patients with cpRBD. PDSS scores on eight sub-items which include overall quality of night's sleep (item 1), maintenance insomnia (item 3), nocturnal restlessness (item 5), distressing nocturnal dreams (item 6), nocturia (item 8), nocturnal cramps (item 11), sleep refreshment (item 14), and daytime dozing (item 15). There was no difference with respect to RLS and nocturnal hallucinations. After adjusting for the effects of age, gender, severity (H&Y stage) and duration of illness in the analysis of covariance, the global PSQI scores, total ESS and PDSS scores were compared between cpRBD and non-cpRBD groups. The cpRBD group was found to have higher global PSQI scores ($P < 0.001$; F: 11.6), higher total ESS scores ($P < 0.0001$; F: 24.1) and higher total PDSS scores ($P = 0.004$; F: 8.6).

Table 2
Sleep scales in Parkinson disease patients with and without cpRBD.

	cpRBD (n = 30)	Non cpRBD (n = 126)	P-value
Global PSQI score	10.1 ± 4.4	6.4 ± 4.1	0.0001
>5 (%) (poor sleeper)	25 (83.3)	48 (38.1)	0.0001
Total ESS score	10.1 ± 3.1	7.3 ± 3.5	<0.0001
>10(%)	18 (60.0)	31 (24.6)	<0.0001
Total PDSS score	101.3 ± 19.8	121.0 ± 16.2	<0.0001
>82 (%)	08 (26.7)	05 (4.0)	<0.0001
Quality of sleep (PDSS sub-item 1)	5.1 ± 2.2	7.1 ± 1.9	<0.0001
Difficulty staying asleep (PDSS sub-item 3)	4.7 ± 2.6	7.2 ± 2.8	<0.0001
Fidgeting in bed (PDSS sub-item 5)	4.8 ± 2.7	7.3 ± 2.6	<0.0001
Distressing dreams (PDSS sub-item 6)	3.7 ± 2.2	9.1 ± 1.6	<0.0001
Nocturia (PDSS sub-item 7)	5.8 ± 2.0	6.8 ± 2.1	0.008
Nocturnal cramps (PDSS sub-item 11)	8.4 ± 2.2	9.4 ± 1.3	0.007
Sleep refreshment (PDSS sub-item 14)	5.2 ± 2.1	7.0 ± 2.0	<0.0001
Daytime dozing (PDSS sub-item 15)	5.1 ± 2.5	6.8 ± 2.1	<0.0001
Numbness/tingling sensation of limbs (PDSS sub-item 10)	9.8 ± 0.9	9.7 ± 0.8	0.262

cpRBD, clinically probable rapid eye movement sleep behavior disorder; PDSS, Parkinson Disease Sleep Scale; ESS, Epworth Sleepiness Scale; PSQI, Pittsburgh Sleep Quality Index.
Values expressed as mean ± SD or number (%).

3.4. Medications

The details of the current medications for PD in patients with and without cpRBD are shown in Supplementary Table 2. There were no statistically significant differences between the two groups.

3.5. cpRBD characteristics

The frequency and characteristics of cpRBD are presented in Table 3. The majority of patients with cpRBD (56.7%) had more than six episodes of RBD per month. The median number of episodes per night was one in 79.3% patients. None of the patients were on medication for cpRBD despite symptoms.

The clinical events were vocalization in the form of talking in almost all the patients, and shouting in 23 patients (76.7%), and crying in three patients (10.0%); two patients (6.7%) laughed during these episodes. None of the patients had episodes of swearing. The motor behaviour was in the form of upper limb movements in the majority of the patients (73.3%). Simple limb movements were predominant (77.3%) and the remaining had complex upper limb movements (22.7%). Lower limb movements were seen in 10 patients (34.5%). Simple and complex limb movements were seen in a similar proportion of patients. Attempts to get out of bed were seen in six patients (20.7%) and two patients (6.9%) had episodes of getting out of bed and walking. None of the patients handled any objects during these episodes.

The majority of patients with cpRBD were able to recall their dreams (96.7%). Dream content included mainly 'chase by animals' in 17 patients (58.6%), and 'chase by mob' in 24 patients (82.8%). Eleven patients had dreams other than chases by animal or mob, such as being on the top of a hill and about to fall, being lost in a forest, being in a house being burgled, and being a patient screaming for help. Dream enactment was in the form of flight response in 21 patients (72.4%), fight response in five patients (17.2%) and both in four patients (10.3%).

Time after falling asleep to the onset of cpRBD was (i) <3 h in eight patients (26.7%), (ii) 3–5 h in 15 patients (50.0%) and (iii) >5 h in seven patients (23.4%). Early morning preponderance of episodes was seen in 11 patients (37.9%). In patients who had onset of cpRBD prior to the motor symptoms, the mean duration of cpRBD onset was 5.25 ± 4.4 years (range, 2–14) and the mean duration of cpRBD was 11.16 ± 5.3 years (range: 5–17). In those who had cpRBD after onset of motor symptoms of PD, the mean duration of cpRBD onset was 3.61 ± 3.6 years (range, 0.5–17) and the mean duration of cpRBD was 2.2 ± 1.9 years (range, 0.5– 8).

4. Discussion

The present study was conducted with the aim to determine the frequency of cpRBD in PD as well as to compare the frequency between the YOPD and OOPD groups. We used the minimal diagnostic criteria for RBD provided in the ICSD-I, which includes the presence of limb or body movements associated with dream mentation, and at least one of the following criteria: harmful or potentially harmful sleep behaviors, dreams appearing to be 'acted out', and sleep behaviors disrupting sleep continuity. Subclinical cases of RBD are diagnosed only by polysomnography. The frequency of cpRBD in our study (19.2%) was comparable to some of the previously reported questionnaire-based studies on the frequency of the RBD in PD (15–47%) [5–7]. The frequency of RBD was high (72%) in the questionnaire-based study by Sinforiani et al. [8], which is an exception. The frequency of RBD as assessed by questionnaire or interview alone is usually lower than assessed by polysomnography (33–58%) [3,27].

Table 3
Characteristics of cpRBD.

Clinical characteristics of RBD	No. (n = 30)	Percentage (%)
Frequency of cpRBD per week		
1	13	43.3
2–3	16	53.3
>3	1	3.3
Frequency of cpRBD per month		
4–6	13	43.3
>6	17	56.7
Vocalization		
Talking	29	96.7
Shouting	23	76.7
Crying	3	10.0
Laughing	2	6.7
Swearing	0	0
Motor behavior		
Upper limb movements	22	73.3
Simple	17	77.3
Complex	5	22.7
Lower limb movements	10	34.5
Simple	5	50.0
Complex	5	50.0
Attempt to get out of bed	6	20.7
Get out of bed and walking	2	6.9
Handling objects	0	0
Vivid dreams	29	96.7
Dream recall	29	96.7
Dream content		
Chase by animal	17	58.6
Chase by mob	24	82.8
Others	11	37.9
Dream enactment		
Fight	5	17.2
Flight	21	72.4
Both	4	10.3
Time of onset during sleep		
<3 h	8	26.7
3–5 h	15	50.0
⩾6 h	7	23.4
Relation to onset of motor symptoms		
Before	6	20.7
With	3	6.9
After	21	72.4

cpRBD, clinically probable rapid eye movement sleep behavior disorder.

It is uncertain whether the frequency of cpRBD differs in those with YOPD compared to those with OOPD. The occurrence of RBD in patients with YOPD has not been systematically studied. RBD has been reported to occur in patients with early-onset parkinsonism (mean age, 51.2 ± 11.6 years) with *parkin* gene mutation. Six out of 10 patients with PARK 2 mutation had RBD (60%) and developed several years (mean delay, 11 ± 8.8 years) after onset of parkinsonism [10]. Lewy bodies and α-synuclein deposition have not been described in Park2 brains. The authors concluded that there are mechanisms other than synuclein deposition that can cause RBD. However, a study by Tuin et al. did not observe RBD in a family with hereditary parkinsonism (PARK 6) [11]. In our study, only four of the 51 YOPD patients had cpRBD. The lower frequency of RBD in young-onset PD in our cohort may be due to relative sparing of pathological changes in brainstem structures causing RBD. Since there was no information on genetic abnormality in this group, further explanation is conjectural; probably there was a predominant non-α-synuclein etiology. This requires further studies with large cohorts of patients with complete genetic evaluation of patients with YOPD to confirm our findings.

Since the frequency of cpRBD in YOPD was low, a comparison with cpRBD in OOPD was not possible. The knowledge of the frequency of cpRBD in YOPD and OOPD separately may also help in prognostication. PD patients with RBD have more non-motor symptoms [3,5,8]. They might have more widespread degenerative changes in the central nervous system than those without RBD [28]. Most of the studies on RBD in PD have reported the occurrence of RBD in patients aged >50 years [7,8]. Similar observation was also seen in the present study.

Male predominance (>85%) has been reported in idiopathic RBD and studies have reported a male predominance in PD patients with cpRBD [6,7]. However, we did not find any significant difference in gender distribution between those PD patients with and without cpRBD, which is similar to previously reported studies [3,8].

Previous studies have reported that cognitive dysfunction and hallucinations or psychosis are predictors of RBD in PD patients [6,8]. In our study, the MMSE scores were similar in PD patients with and without cpRBD, an observation also noted in previous studies [29]. We acknowledge that subtle cognitive dysfunction in PD may have escaped detection by MMSE. Though our patients were not specifically queried regarding the presence of visual hallucinations but as a sub-item in the PDSS, the presence of nocturnal hallucinations was similar in both groups.

In the present study, the presence of cpRBD in PD inversely correlated with the tremor score and its proportion of total UPDRS motor score, which is consistent with previous observations [3,29]. The exact reason for the lower prevalence of cpRBD in patients with tremor-predominant PD is unknown. However, it has been reported that the presence of tremor is associated with fewer non-motor symptoms such as olfactory dysfunction and slower progression [29]. Studies have demonstrated increased incidence of falls in PD patients with RBD similar to that in the present study, along with more axial signs [3]. A greater proportion of PD patients with cpRBD had advanced stage of PD (H&Y >2) similar to the observation by Scaglione et al. [7]. RBD symptoms vary in time and may disappear as the disease progresses, as demonstrated by longitudinal follow-up studies [5]. Patients with RBD were receiving a higher mean dose of levodopa [29]. However, there was no difference in terms of levodopa dosage in present study, similar to other studies [8].

Some studies have reported the occurrence of RBD preceding motor parkinsonism in 18–52% of PD patients [3,6]. This has been explained based on the Braak staging system for PD which suggests the early involvement of pontine (locus ceruleus) and medullary nuclei by Lewy body pathology prior to substantia nigra involvement. However, most patients develop RBD after the onset of motor symptoms [5,6], which was also documented in our study (72.4%). cpRBD episodes occurred frequently (two or three nights a week) in >50% patients in the present study, which is more as compared with one other study (35.5%) [7].

The most common theme of dreams in patients with RBD in our study was defensive action of the sleeper against attack by flight response (70.4%). Vocalization in the form of talking was most frequent during RBD episodes, similar to previous reports [7]. Sleep-related injuries have been reported in a previous study [7] ranging from 33% to as high as 69.4%. The same was not observed in the present study.

Sleep disorders are frequent in PD and the etiology of sleep problems is not well understood. They may arise from the pathology of the disease or from other disease-related factors such as motor dysfunction, dopaminergic medication, and mood disturbances [30,31]. PDSS is a useful scale for bedside quantification of sleep problems in PD [19]. We used PSQI to determine the quality of sleep, ESS to determine daytime sleepiness and PDSS score in our cohort of patients [20,21]. In our study, the total PDSS score, total ESS score and global PSQI were significantly higher in patients with RBD. These findings remained significant even after adjusting for the effects of age, gender, H&Y stage, and duration of illness

which are also confounding factors for sleep disturbances in patients with PD. This study found an independent association of poor sleep quality with the presence of RBD in patients with PD.

Patients with cpRBD had excessive daytime sleepiness (60%), poor sleep quality, poor sleep efficiency, daytime dysfunction and reduced sleep duration, which was consistent with other studies [6,9].

Depression and anxiety are associated with sleep disturbances in patients with PD and it is extremely important to diagnose these treatable conditions [31]. The mean HAM-A and HAM-D score were significantly correlated with PSQI, PDSS and ESS in patients with cpRBD. This suggests that severity of anxiety and depression correlated with poor sleep quality and excessive daytime somnolence in patients with cpRBD.

The study had several limitations. First, it was a questionnaire-based study and the diagnosis of cpRBD was based on the patient's ability to recall the events. Second, there was an element of selection bias and small sample size of young-onset PD. Third, there was lack of polysomnographic confirmation of RBD and lack of sleep apnoea questionnaire usage required to exclude patients with sleep apnoea. Finally, the association of cpRBD with other non-motor manifestations of PD such as psychosis, cognitive disturbances and autonomic dysfunction were not studied. Future studies should investigate the frequency of RBD in a larger cohort young-onset PD to confirm our findings, and polysomnography should be done to rule out other sleep disorders that mimic RBD, such as obstructive sleep apnoea and night terrors.

This study demonstrated that the older-onset PD had a higher frequency of RBD than young-onset PD. To conclude, patients with cpRBD were older with later-onset motor symptoms, longer duration of disease, more axial signs, fewer tremor symptoms, poor sleep quality and efficiency, and more frequent daytime sleepiness. It is important to carefully interview each PD patient and caregiver for symptoms of RBD.

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None.

Conflict of interest

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: http://dx.doi.org/10.1016/j.sleep.2014.01.022.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.sleep.2014.01.022.

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